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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/147,947	Applicant(s) TSURUOKA ET AL.	
	Examiner William W. Moore	Art Unit 1652	

-- Th MAILING DATE of this communication appears on the cover sheet with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-10, 12, 14-19, and 21-59* is/are pending in the application.

4a) Of the above claim(s) *10 and 17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-9, 12, 14-16, and 21-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *10 and 17-19* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Response to Amendment

Applicants' Amendment D, Paper No. 13, has been entered and claims 1-4, 11, 13 and 20 were deleted at Applicants' request. The amendments overcome the rejection of record of claim 9 under 35 U.S.C. §101. It is noted that the non-elected claims 10 and 17-19 subject to the restriction requirement stated at pages 2-5 of Paper No. 11 mailed September 12, 2000, remain in the application.

Claim Rejections - 35 USC §101

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5, 6, 14-16 and 21 remain rejected for reasons of record under 35 U.S.C. §101 because the claimed invention is directed to non-statutory subject matter.

Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. The prosecution histories of the patents that Applicants cite at page 11 of Paper No. 13 are not germane to the claims herein. Each of claims 5, 6 and 14-16 describes a DNA that, unaltered by any person, exists in cells of persons living all over the planet. Claim 21 describes a protease present in persons, unaltered by anyone. Naturally-occurring compositions of matter are not statutory subject matter and amending claims 5, 6, 14-16 and 21 to distinguish the DNAs and the protease from compositions of matter present in Nature by describing their isolation from Nature will overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-9, 12, 14-16, and 26-59 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' introduction of claims 21-30 and 57-59 and amendments of claims 6 and 14-16 necessitate this new ground of rejection. It is clear that recitations of the amended and the newly-submitted claims are not artifacts of translation. Applicants actually intend to describe a "peptide having serine protease, domain, or their partial peptide activity", in claim 6, and to describe "its partial peptide", in each of claims 21-24, in an attempt to reach multiple amino acid sequence embodiments differing both in amino acid sequence from the integral neurotrypsin of SEQ ID NO:6, and from its discrete domains separately described in claims 22-24, and in the size, or length, of amino sequence. There is no disclosure in the specification of a partial peptide having the activity of a serine protease other than the serine protease domain that comprises the amino acid sequence region from position 578 to position 822, inclusive, of SEQ ID NO:6. Since claims 6 and 22 both describe this region as a domain, it cannot also be a "partial peptide" of the same claims. There is no disclosure in the specification of any other partial peptide of SEQ ID NO:6 having the activity of a serine protease and no disclosure of any partial peptide that might have the activity of a kringle domain other than the amino acid sequence region of SEQ ID NO:6 consisting of positions 40 to 112, inclusive, of SEQ ID NO:6. Similarly, the specification lacks any disclosure of partial peptides that might have the activity of a scavenger receptor cysteine-rich domain [SRCR] other than the four regions of SEQ ID NO:6 consisting of positions 117 through 217, inclusive, positions 227 through 327, inclusive, positions 334 through 433, inclusive, and, positions 447 through 547, inclusive.

The specification fails to exemplify or describe the preparation of any other partial peptide. Neither the specification nor the prior art of made of record herein demonstrate that such undisclosed and undefined partial peptides may be expressed separately, or as a

fusion partner, in recombinant host cells in any fashion which will permit the peptide to meet the functional limitations of the claims. The specification does not otherwise disclose or suggest the nature or source of partial peptides that meet the claim limitations. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of partial peptides that can function as required, nor any other characteristic that permits a correlation between the structure of any alternative, prospective, partial peptide and the functions performed by the discrete domains of SEQ ID NO:6 that the specification identifies: the serine protease domain of positions 578 through 822, the kringle domain at positions 40 through 112, and the SRCR domains at positions 117 through 217, positions 227 through 327, positions 334 through 433, and positions 447 through 547.

A further written description issue flows from the recitations of "partial peptides" where the prospective nucleic acid sequences that encode these prospective amino acid sequences are the basis for describing further, prospective, nucleic acid species by hybridization under stringent conditions. The specification discloses only one species of nucleic acid that hybridizes with the nucleic acid sequence of SEQ ID NO:6, the murine BSSP cDNA of Example 1 Applicants used to identify the human cDNA. Applicants' use of stringent conditions in this identification of the nucleic acid sequence of the murine BSSP cDNA disclosed by Gschwend et al. in the prior art is not challenged. Yet claims 6, 12, 27-30, 34-36, 40-43, 47-50 and 57-59 all describe DNAs, or their uses, that need not hybridize to SEQ ID NO:6, but may hybridize as well to undefined and undisclosed "partial peptides" and also to undefined and undisclosed nucleic acid sequences that

encode a myriad of divergent amino acid sequences. The Court of Appeals for the Federal Circuit has determined that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The only nucleic acid sequence that the specification shows Applicants to have possessed in addition to SEQ ID NO:5, which encodes SEQ ID NO:6, at the time the priority document was filed for this application is SEQ ID NO:3. But SEQ ID NO:3 is in the prior art, thus cannot be a claimed invention. Even if Applicants had disclosed or suggested "a method for obtaining" a nucleic acid that encoded amino acid sequences other than SEQ ID NO:6 and the six discrete domains that Applicants identity therein, nothing demonstrates that they were "able to envision" enough of the "structure of" a divergent claimed product to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). Other than the disclosure of SEQ ID NO:3, the specification's treatment of the subject matters of claims 6, 12, 27-30, 34-36, 40-43, 47-50, and 57-59 is entirely prospective and skilled artisans in the relevant fields of molecular biology and mammalian genetics could not predict the structure, or other properties, of claimed DNAs that might support practice of the invention of these claims.

Claims 5-10, 12, 14-19 and 21-59 remain rejected for reasons of record under 35 U.S.C. §112, first paragraph, because the specification, while being enabling (a) for the preparation of a human neurotrypsin/BSSP of claim 1 **consisting of** the amino acid sequence of SEQ ID NO:6 and for a nucleotide sequence that encodes it, (b) for the preparation of a functioning serine protease domain of a human neurotrypsin/BSSP of claim 2 **comprising** the amino acid sequence region from position 578 to position 822, inclusive, of SEQ ID NO:6 and for a nucleotide sequence that encodes it, (c) for the preparation of an active kringle domain of a human neurotrypsin/BSSP of claim 3 **comprising** the amino acid sequence region from position 40 to position 112, inclusive, of SEQ ID NO:6 and a nucleotide sequence that encodes it, (d) for the preparation of a

functioning scavenger receptor cysteine-rich domain of a human neurotrypsin/BSSP of claim 4 **comprising an amin acid sequence regi n selected from the group of regions consisting of** (i) position 117 to position 217, inclusive, of SEQ ID NO:6, (ii) position 227 to position 327, inclusive, of SEQ ID NO:6, (iii) position 334-433, inclusive, of SEQ ID NO:6 and, (iv) position 447 to position 547, inclusive, of SEQ ID NO:6, as well as for nucleotide sequences that encodes each, and, (e) for the use of the human neurotrypsin/BSSP of SEQ ID NO:6 of claim 1, and a nucleotide sequence that encodes it of claim 13, in processes for screening physiologically active substances that have some certain, recognizable, result,

does not reasonably provide enablement for the myriad of partial peptides of each of the native human neurotrypsin/BSSP and its various domains wherein unspecified portions are altered by undescribed amino acid sequence substitutions, deletions and/or additions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Recitations of newly-submitted claims 21-24 do not exclude the arbitrary assignment of any number of amino acid insertions, deletions, or substitutions in the overall neurotrypsin amino acid sequence and certain of its domains. For this reason as well, the prior art rejections of record are maintained. The specification describes no specific locations for substitutions, deletions or insertions anywhere in the amino acid sequence of SEQ ID NO:6, describes no substituents, and entirely fails to support random introduction of amino acid insertions, deletions, or substitutions anywhere, in any combination or any pattern, in the native serine protease of SEQ ID NO:6 or its separate domains that will predictably permit the protease, or its several domains, to function. Applicants arguments fail to address the standard set by the CCPA, the predecessor of the present Court of Appeals for the Federal Circuit, which held that "mak[ing] and screen[ing]" any and all possible alterations cannot be considered enabling because a reasonable correlation must exist between the scope of **guidance** provided by the specification and the scope asserted in the claimed subject matter. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency

of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The instant specification provides no guidance whatsoever for amino acid sequence alterations and the standard set by the CCPA has been approved by the Federal Circuit in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Neither the prior art made of record herewith nor Applicant's specification can identify a single amino acid in the primary sequence of SEQ ID NO:6, or any other mammalian serine protease that might be altered. Neither does the prior art made of record herewith nor Applicant's specification teach the nature of an alteration that may be made which will permit a resulting polypeptide to function as a serine protease, a kringle domain or a scavenger receptor cysteine-rich domain.

Applicants' arguments in Paper No. 13 also fail to address the decision by the Federal Circuit in *Genentech, Inc. v. The Wellcome Found. Ltd.*, 29 F.3d 1555, 31 USPQ2d 1161 (Fed. Cir. 1994). After considering whether definitional statements might enable a claim scope argued to extend beyond a disclosed, recombinantly-produced, gene product having its native amino acid sequence to embrace a specific variant gene product encoded by a specifically-altered DNA sequence, the court held that only a narrow structural and functional definition was enabling precisely because the sweeping definitions of scope in the patent specification could not reasonably have been relied upon by the PTO in issuing the patent. *Genentech*, 29 F.3d 15 at 1564-65, 31 USPQ2d at 1168. Mere sequence perturbation cannot enable the design and preparation of nucleotide sequences of claims 5, 6 and 14-16, which in turn encode the myriad of divergent polypeptides of claims 21-24, and also encode products that retain a recognizable function. The rejection of record is sustained with respect to the non-enabled scope of variegation described for the claimed neurotrypsin, its several domains, DNAs encoding same, and expression vectors and host

cells comprising such DNAs, and methods of use of the divergent neurotrypsin, its several domains, and encoding DNAs and vectors and host cells comprising them.

Claims 8, 9 and 44-50 present a further issue of enablement because, in addition to describing the preparation of a human neurotrypsin by culturing host cells maintaining an expression vector, each claim recites "breeding". This term describes the selected union of separate animals either of which must arise from a zygote - which is a single cell and may be transformed with an expression vector - to yield progeny expressing the neurotrypsin. While it is agreed that both prokaryotic and eukaryotic **host cells**, including vertebrate cells in culture, may be transformed or transfected with an expression vector maintaining a DNA encoding a human neurotrypsin, the specification provides no guidance whatsoever for producing a transgenic animal that expresses a transforming, human neurotrypsin-encoding DNA. Applicants' arguments in Paper No. 13 fail to address the holding of *Wands* that the first paragraph of 35 U.S.C. §112 requires a disclosure to enable one of skill in the art to practice the invention as claimed without undue experimentation and that a rejection under 35 U.S.C. §112, first paragraph, for non-enablement is supported where unpredictability in an attempt to practice a claimed invention is a significant factor. 8 USPQ2d at 1404 (Fed. Cir. 1988). Neither the specification nor the prior art of record supports such "breeding". The rejection of record is sustained with respect to such methods of "breeding" to prepare the disclosed neurotrypsin of SEQ ID NO:6, as well as the myriad variants embraced by the claims, where an artisan would require extensive, undue, experimentation to determine how to transform a zygote with a disclosed DNA to ensure that the encoded neurotrypsin could be expressed in central nervous system tissue or any other tissue. It is again noted that limiting claims 5-10, 12, 14-19 and 21-59 as indicated in the statement spanning pages 2 and 3 above will avoid the prior art cited hereinbelow as well as the following rejection under the second paragraph of the statute.

Claims 5-9, 12, 14-16 and 21-59 are, essentially for reasons of record, rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants present no argument addressing the rejection of record under 35 U.S.C. §112, second paragraph, because they considered that the claim amendments of Paper No. 13 resolved any ambiguities in the claims. Yet the recitations in claim 6 of "their partial peptide" and in claims 21-24 of "its partial peptide" describe a narrow range or limitation that falls within the broad range or limitation - a full-length neurotrypsin amino acid sequence in claim 21 and its integral domain amino acid sequences in claims 22-24 - in these same claims thus are indefinite since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Partial peptides of claims 21-24 may be of any length, and indeed may be equal in length to, or have a length greater than or less than, the domains specifically recited in the claims where combinations of amino acid modifications are made according to the terminal clauses of each claim. In addition to partial peptides which may be of any length, a domain of claim 6 is also a partial peptide of SEQ ID NO:6. See, *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), wherein broad language followed by "such as" and then narrow language was held to render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. See also, *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). Claims 5, 7-9, 12, 14-16 and 25-59 are included in this rejection because they depend from claims 6 and 21-24 but do not resolve the ambiguity present in the independent claims.

Claim 24 is independently rejected as indefinite because "cysteine" is misspelled at line 1 of the claim. Claims 14-16, 28-30 and 44-59 are independently rejected as indefinite because each recites "the domain or their partial peptides"; the recitations lack standard

English grammar and are ambiguous because **a** domain is a singular entity, rather than a plural entity as required by the subsequent recitation of "their".

Claim Rejections - 35 USC §§102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 5-9, 12, 14-16, 21-24 and 28-43 are for reasons of record rejected under 35 U.S.C. §102(a) as being anticipated by Gschwend et al., **Molecular and Cellular Neuroscience**, Vol. 9, pages 207-219, published July 23, 1997, a day in advance of Applicants' foreign priority date. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Gschwend et al. disclose, the amino acid sequence and encoding DNA sequence of the murine neurotrypsin, the same amino acid sequence set forth in SEQ ID NO: 4 herein. The murine neurotrypsin amino acid sequence - and its coding sequence, SEQ ID NO:3 herein - anticipates the claimed subject matters because the specification teaches that SEQ ID NO:3 hybridizes with SEQ ID NO:5 and the amino acid sequence of SEQ ID NO:4 has 66.4% similarity with the amino acid sequence of SEQ ID NO:6 herein, containing many extensive partial peptides differing by but a few amino acid substitutions, deletions, and/or additions from SEQ ID NO:6.

Claims 5-9, 12, 14-16, 21-24 and 28-43 are for reasons of record rejected under 35 U.S.C. §102(e) as being anticipated by Au-Young et al., U.S. Patent No. 5,869,637,

available as prior art by virtue of its July 22, 1996, filing date who disclose the amino acid sequence of a human kallikrein, a serine protease, SEQ ID NO:1, and its encoding DNA, SEQ ID NO:2. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims dependent thereon are included in this rejection in view of the recitation, "or its partial peptide", at line 1. The protease of Au-Young et al. shares 39% amino acid sequence similarity with the human neurotrypsin protease domain present in SEQ ID NO:6 herein and comprises extensive partial peptides differing by "at least one" amino acid substitution, deletion, and/or addition from the human neurotrypsin protease domain of SEQ ID NO:6 and claim 22. Because such partial peptides are described by claims herein as the basis for identifying nucleic acids that may hybridize to nucleic acids encoding the partial peptides - as well as divergent peptides - SEQ ID NO:2 of Au-Young et al. is considered to be within the scope of claims 5, 6, 14-16 and 28-30. Au-Young et al. further disclose, cols. 8-12, the preparation of both an expression vector comprising a DNA encoding this kallikrein and a host cell transformed with the expression vector.

Claims 5-9, 12, 14, 21, 22, 28, 31, 34, 37 and 41 are for reasons of record rejected under 35 U.S.C. §102(b) as being anticipated by Fujikawa et al., **Biochemistry**, Vol. 25, pages 2417-2424, who disclose the human blood coagulation factor XI, a serine protease, and its encoding DNA, see Figure 2. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims dependent thereon are included in this rejection in view of the recitation, "or its partial peptide", at line 1. The protease domain of human factor XI shares 33% amino acid sequence similarity with the protease domain of human neurotrypsin set forth in SEQ ID NO:6 herein and comprises extensive partial peptides that differ by "at least one" amino acid substitution, deletion, and/or addition from the human neurotrypsin protease domain

of claim 22. Fujikawa et al. further disclose, pages 2418-2420, the preparation of an expression vector comprising DNA encoding the human factor XI protease and of a host cell transformed with the vector.

Claims 5-9, 12, 15, 21, 29, 32, 35, 38 and 42 are for reasons of record rejected under 35 U.S.C. §102(b) as being anticipated by Wood et al., WO 96/03644, who disclose the human mlk receptor tyrosine kinase, SEQ ID NO:2 and its encoding DNA, SEQ ID NO:1. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims dependent thereon are included in this rejection in view of the recitation, "or its partial peptide", at line 1. The human mlk receptor tyrosine kinase kringle domain shares 34% amino acid sequence similarity with the kringle domain of human neurotrypsin set forth in SEQ ID NO:6 herein and comprises extensive partial peptides differing by "at least one" amino acid substitution, deletion, and/or addition from the human neurotrypsin kringle domain of claim 23. Because such partial peptides are described by claims herein as the basis for identifying nucleic acids that may hybridize to nucleic acids encoding the partial peptides - as well as divergent peptides - SEQ ID NO:2 of Au-Young et al. is considered to be within the scope of claims 5, 6, 14-16 and 28-30. Wood et al. further disclose, pages 34-39, the preparation of expression vectors comprising DNAs encoding human and murine mlk receptor kinases, and of host cells transformed with the expression vectors, for recombinant production of both human and murine enzymes.

Claims 5-9, 12, 15, 21, 29, 32, 35, 38 and 42 are rejected under 35 U.S.C. §102(e) as being anticipated by Anderson et al., U.S. Patent No. 5,714,145, who disclose the human serine protease tissue plasminogen activator [tPA], see Figure 2, and inherently disclose an encoding DNA sequence. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims

dependent thereon are included in this rejection in view of the recitation, "or its partial peptide", at line 1. The kringle-2 domain of human tPA shares 32% amino acid sequence similarity with the kringle domain of human neurotrypsin set forth in SEQ ID NO:6 herein and comprises extensive partial peptides that differ by "at least one" amino acid substitution, deletion, and/or addition from the human neurotrypsin kringle domain of SEQ ID NO:6 and claim 23. They also disclose, cols. 13-18, preparation of expression vectors comprising a DNA encoding the human tPA and of host cells transformed with the expression vectors.

Claims 5-9, 12, 15, 21, 24 and 30 are rejected under 35 U.S.C. §102(e) as being anticipated by Elshourbagy et al., U.S. Patent No. 5,916,766, who disclose macrophage scavenger receptors of human and murine origin, SEQ ID NOs:2 and 7, DNA encoding the human receptor and, cols. 38-41, expression vectors and transformed host cells comprising the encoding DNA. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims dependent thereon are included in this rejection in view of the recitation, "or its partial peptide", at line 1. The murine scavenger receptor cysteine-rich domain [SRCR], positions 394-489, shares 31% amino acid sequence similarity with the human neurotrypsin SRCR domain 1, amino acid positions 117-217, set forth in SEQ ID NO:6 herein, comprising extensive partial peptides that differ by "at least one" amino acid substitution, deletion, and/or addition from the human neurotrypsin SRCR domain 1 of claim 24.

Claims 5-9, 12, 15, 21, 24, 30, 33, 36, 39 and 43 are rejected under 35 U.S.C. §102(e) as being anticipated by Krieger et al., U.S. Patent No. 5,510,466, who disclose, Fig. 3, a bovine macrophage scavenger receptor and DNA encoding the receptor. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims dependent thereon are included in this rejection in view

of the recitation, "or its partial peptide", at line 1. The bovine SRCR domain, positions 352-452, shares 58% amino acid sequence similarity with the human neurotrypsin SRCR domain 2, amino acid positions 227-327 of SEQ ID NO:6 herein, comprising extensive partial peptides differing from the human neurotrypsin SRCR domain 2 of claim 24 by "at least one" amino acid substitution, deletion, and/or addition. They also disclose, cols. 17 and 18, preparation of expression vectors and transformed host cells comprising a DNA encoding the receptor.

Claims 5-9, 12, 15, 21, 24, 30, 33, 36, 39 and 43 are rejected under 35 U.S.C. §102(e) as being anticipated by Krieger et al., U.S. Patent No. 5,624,904, who disclose another bovine macrophage scavenger receptor and DNA encoding the receptor, SEQ IDs NOs:2 and 1. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims dependent thereon are included in this rejection in view of the recitation, "or its partial peptide", at line 1. This bovine receptor's SRCR domain, positions 350-449, shares 52% amino acid sequence similarity with the SRCR domain 3, amino acid positions 334-432 of human neurotrypsin set forth in SEQ ID NO:6 herein, comprising extensive partial peptides differing by "at least one" amino acid substitution, deletion, and/or addition from the SRCR domain 3 of human neurotrypsin of claim 24. Krieger et al. also disclose, cols. 12 and 13, preparation of expression vectors and transformed host cells comprising a DNA encoding the receptor.

Claims 5-9, 12, 15, 21, 24, 30, 33, 36, 39 and 43 are rejected under 35 U.S.C. §102(e) as being anticipated by Koths et al., U.S. Patent No. 5,624,904, who disclose a human macrophage scavenger receptor and DNA encoding the receptor, SEQ IDs NOs:10 and 9. Applicant's arguments filed March 12, 2001, have been fully considered but they are not persuasive. Claim 21 and claims dependent thereon are included in this rejection in view of the recitation, "or its partial peptide", at line 1. The

SRCR domain of this human receptor, positions 24-123, has 52% amino acid sequence similarity with the SRCR domain 4, amino acid positions 447-547 of human neurotrypsin set forth in SEQ ID NO:6 herein, comprising extensive partial peptides differing by "at least one" amino acid substitution, deletion, and/or addition from the human neurotrypsin SRCR domain 4 of claim 24. They also disclose, cols. 21 and 23, preparation of expression vectors and transformed host cells comprising a DNA encoding the receptor.

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

Claims 25-27 and 44-59 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gschwend et al., in view of Au-Young et al.('637).

The disclosures of Gschwend et al. of the cloning of a cDNA encoding a murine neurotrypsin, discussed hereinabove, are taken as before and their further disclosures are now cited of screening, see Fig. 7, for expression of the message encoding the protease in regions of the brain engaged in processing and storage of learned behaviors and memories, regions where, p. 216, tPA and uPA are also expressed and also are associated with learning processes. The disclosures of Au-Young et al. are also taken as before and their further teachings, cols. 8-11, of preparing expression vectors and transformed host cells comprising a human serine protease-encoding cDNA in order to practice a process for preparing the serine protease, are now cited as well as the teaching, col. 15 at lines 13-34,

of using the recombinantly-produced serine protease in screening therapeutic compounds. It would have been obvious to one of ordinary skill in the art at the time the invention was made to insert the neurotrypsin-encoding DNA sequence of Gschwend et al., into any of the various expression vectors of Au-Young et al. and to transform any of the various host cells of Au-Young et al. with the corresponding expression vector in order to practice a process for preparing the neurotrypsin, as well as practicing subsequent processes of using the recombinantly-produced serine protease in screening therapeutic compounds. This is because such an artisan at that time would have had a reasonable expectation of success in recombinantly expressing the neurotrypsin using such expression vectors and transformed host cells in view of their common use for that purpose evidenced in the teachings of Au-Young et al. This is also because such an artisan at that time would have been motivated to recombinantly express the neurotrypsin in order to practice a process of screening therapeutic compounds where Gschwend et al. teach that many well-known extracellular serine proteases common to all mammals are expressed in the nervous system of mammals and play critical roles in mediating neural plasticity, even in the brains of adult mammals.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached from 8:00AM-6:30PM EST on Mondays, Wednesdays, and Fridays and from 11:30AM-6:00PM EST on Tuesdays and Thursdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804.

The fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
May 21, 2001

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